REMARKS

Claims 1-31 and 33-49 were pending. Claims 1-31, 33-42 and 45-49 were examined as part of the invention of Group I. Claims 43 and 44 have been withdrawn pursuant to a previous Restriction Requirement, which was traversed.

Applicants note with gratitude the Examiner's removal of the outstanding 35 U.S.C. §§ 103 and 112 rejections. Applicants respectfully submit that a *Notice of Allowance* is now in order.

However, an *Office Action* was mailed July 28, 2005 instead, which required a new restriction to one of the following 9 New Groups (hereinafter, the "New Restriction Requirement"):

Group I	Claims 1-21, 24-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is gold; the ligand is NxS4-x wherein x = 1; targeting moiety is SEQ ID No. 2; the disease is a neurological disease; and the disease is assessed by nuclear magnetic resonance imaging.
Group II	Claims 1-15, 17-21, 24-31, 33-42 and 45-49 (in-part), drawn to a product, methods of making the product, and uses of a product wherein the metal support is silver; the ligand is NxS4-x wherein x = 0; targeting moiety is SEQ ID No. 1; the disease is an oncological disease; and the disease is assessed by positron emission tomography.
Group III	Claims 1-15, 17-21, 24-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is copper; the ligand is NxS4-x wherein x = 2; targeting moiety is SEQ ID No. 3; the disease is an inflammatory disease; and the disease is assessed by single photon emission computed tomography.
Group IV	Claims 1-15, 17-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is Tc; the ligand is NxS4-x wherein x = 3; targeting moiety is bombesin 7-14; the disease is an infection; and the disease is assessed by ultrafast x-ray computed tomography.

Group V	Claims 1-15, 17-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is Re; the ligand is NxS4-x wherein x = 0; targeting moiety is a dopamine receptor; the disease is an oncological disease; and the disease is assessed by positron emission tomography.
Group VI	Claims 1-15, 17-21, 24-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is Mn; the ligand is NxS4-x wherein x = 1; targeting moiety is a serotonin receptor; the disease is a neurological disease; and the disease is assessed by digital subtraction angiography.
Group VII	Claims 1-15, 17-21, 24-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is Fe; the ligand is NxS4-x wherein x = 2; targeting moiety is a nicotinic receptor; the disease is an inflammatory disease; and the disease is assessed by positron emission tomography.
Group VIII	Claims 1-15, 17-21, 24-31, 33-42 and 45-49 (in-part), drawn to product, methods of making the product, and uses of a product wherein the metal support is Ni; the ligand is NxS4-x wherein x = 3; targeting moiety is a GABA receptor; the disease is an infection; and the disease is assessed by single photon emission computed tomography.
Group IX	Claims 43 and 44, drawn to products, a method of preparation of a support surface for manufacturing a complex forming metal labeling agent.

As explained below in detail, Applicants strenuously object to the New Restriction Requirement. However, solely to avoid abandonment for failure to respond, and without acquiescing to the merits of the New Restriction Requirement, Applicants would be willing to elect, with traverse, a modified version of New Group II, drawn to a product, methods of making the product, and uses of a product wherein the ligand is NxS4-x wherein x = 3 (not 0 as proposed); targeting moiety is SEQ ID No. 1; the disease is an oncological disease; and the

complex forming metal ion is a radioactive metal. Applicants note that New Group II was indicated to include 1-15, 17-21, 24-31, 33-42 and 45-49 (in-part).

Irrespective of the election made, Applicants respectfully request that the New Restriction Requirement be favorably reconsidered and withdrawn and respectfully submit that all of the previously examined claims 1-31, 33-42 and 45-49 as presently pending should be kept together instead of further separated because, as discussed below, all of the pending claims define a single, unified invention. For example, attempting to require restriction to the various metal supports as claimed (*e.g.*, gold, silver, copper) is inappropriate because none of them are patentable over each other (*i.e.*, a prior art search would yield them all together, such that no one metal would be patentable over the others). Furthermore, none of the previously examined Group I claims, 1-31, 33-42 and 45-49 are distinct or patentable over each other. Thus, there is no basis to maintain this New Restriction Requirement.

A. The New Restriction Requirement is Improper

The current 9-way New Restriction Requirement appears to have been created by simply making into a separate New Group various possible combinations of the metal support, the chelator, the targeting moiety, the disease or disorder or abnormal physical state and the method of assessing the disease or disorder or abnormal physical state. However, no explanation was provided as to why all of these New Groups are distinct from each other. MPEP § 816.

For example, no basis was given for why New Group I (wherein the metal support is gold), New Group II (wherein the metal support is silver) and New Group III (wherein the metal support is copper) are distinct from each other when the Specification explains, and the New Restriction Requirement does not dispute, that such compounds are all metals that can

function as the metal support contemplated by the present claims. *See, e.g.*, Specification, p. 7, lines 15-19. Nor is it explained in the New Restriction Requirement why a single search of all of the claimed compounds with similar structures and properties, *e.g.*, different chelators and different targeting peptides, together would be a significant burden on the USPTO in light of their similarities. The conclusion that there is no such significant burden on the USPTO is underscored by the fact that the USPTO has been examining the prior art with no difficulty since its initial *Office Action* of November 21, 2003.

Nor is it explained in the New Restriction Requirement why the search of compounds capable of targeting of each of, *e.g.*, a neurological disease, an oncological disease, an inflammatory disease or an infection, should necessitate their formation into a separate New Group.

Moreover, as a result of the GATT legislation limiting the term of a patent to twenty years from its effective filing date, the unjustified delay in the examination of the non-elected claims will likely result in the patent term for those claims being unnecessarily shortened. This injustice is further exacerbated by the lack of any explanation as to why the instant New Restriction Requirement was issued nearly two years after the original Restriction Requirement was mailed, and after substantial prosecution, expenses and resources have already been expended.

Under the New Restriction Requirement, it would be necessary for the USPTO to conduct a duplicate, redundant search 9 times for each of those 9 divisional applications. Moreover, the New Restriction Requirement suggests that the present invention can be restricted to even more than 9 New Groups, although no further New Groups have been specified. *See Office Action*, p. 4 ("[T]his list is not exhausted"); *see also* the "in part" language in the

description of each New Group. If a different Examiner is assigned to any of the divisional applications, an even more significant loss of USPTO resources and time will be incurred as a result of the examination of those divisional cases. Thus, Applicants respectfully submit that this proposal will result in a significant and unnecessary drain of USPTO resources. Accordingly Applicants respectfully submit that the New Restriction Requirement is improper and should be withdrawn.

B. The Premise Behind the New Restriction Requirement is Incorrect

It is further respectfully submitted that the premise behind the New Restriction Requirement is additionally improper. As an initial matter, the presently pending claims are linked so as to form a single general inventive concept: all of the claims require compositions comprising a metal support surface and a conjugate (comprising a ligand and a targeting molecule) releasably bound to the metal support surface wherein the conjugate coordinates with a complex forming metal ion so that the metal ion labeled conjugate is released from the support surface (and additionally, kits or methods for preparation thereof). The Examiner's assertion that the claims lack unity of invention because "[t]he groups of inventions claimed contain a metal support which does not define a contribution over the prior art" (*Office Action*, p. 5) is clearly incorrect. As explained in detail in Applicants' *Amendment and Response to Office Action* filed April 28, 2005, the claimed invention with the metal support does define a contribution over the prior art, as illustrated by the Examiner's withdrawal of the obviousness rejection over U.S. Patent No. 6,027,711 to Sharma et al. *Amendment and Response to Office Action* filed April 28, 2005, at, *e.g.*, pages 17-20.

Furthermore, the present invention has been either mischaracterized or misunderstood by the Examiner. For example, the New Restriction Requirement separates New Groups IV and V on the basis of Tc and Re as a metal support respectively. However, the claims and the Specification teach the use of Tc and Re as complex-forming metals, not metal supports. Specification, p. 1, lines 10-11; p. 12, line 10-12 ("The term "support surface" refers to any substrate that is insoluble and inert in labeling solution and is a metal support surface which is either made of, or is coated with, gold, silver or copper ...").

Similarly, the Examiner has included SEQ ID NO: 1 and bombesin 7-14 in separate groups (New Groups I and IV); however, these are the same sequence. Additionally, although the application teaches a preference for use of a radioactive complex forming metals and for use of ^{186} Re, ^{188}Re and ^{99m}Tc in particular, the Examiner has restricted the New Groups to positron emitters only; thus effectively ignoring the radioactive metals which emit for example, beta or gamma rays, including the preferred ^{186} Re, ^{188}Re and ^{99m}Tc. Specification, p. 13, lines 1-23. Applicants respectfully submit that all radioactive metals can be searched together, as evidenced from the prosecution to date in the present application.

Applicants also respectfully submit that the Examiner's apparent suggestion that performing a search for the various diseases and uses place a significant burden on the USPTO is incorrect. These limitations are not part of any independent claims, but are rather additional limitations in additional dependent claims (*e.g.*, 26, 27, 33, 47, 48, 49). All that is required for these additional dependent claims to be patentable over the prior art is that independent claim 1 (which was obviously easy to search) is patentable. Furthermore, Applicants have proven the patentability of claim 1 in their *Amendment and Response to Office Action* of April 28, 2005.

As such, withdrawal of the New Restriction Requirement is respectfully requested.

CONCLUSION

In light of the present amendments and remarks, Applicants respectfully submit that the present claims are in condition for allowance, early notice of which is earnestly sought. If any outstanding issues remain, the Examiner is invited to telephone Applicants' undersigned attorneys at her convenience at the number provided below.

No fees, other than the fee for extension of time to respond, are believed to be required for the filing of this *Response to Office Action.* However, please charge any additional required fees, and credit any overpayments, to Deposit Account No. 50-0540.

Respectfully submitted,

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